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## **Interventions for Deliberately Altering Blood Pressure in Acute Stroke**

Chamila M. Geeganage and Philip M.W. Bath

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## Interventions for Deliberately Altering Blood Pressure in Acute Stroke

Chamila M. Geeganage, MB, BS, MSc; Philip M.W. Bath, MD, FRCP

**H**igh blood pressure (BP) is common in both acute ischemic stroke and primary intracerebral hemorrhage. Both high and low BP are associated with a poor outcome. Hence, drugs that elevate a low BP or reduce a high BP might be beneficial. We systematically assessed the effect of deliberate BP-altering in patients with acute stroke.<sup>1</sup>

### Search Strategy

We searched the Cochrane Stroke Group Trials Register, the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and other databases, reference lists of relevant publications, and contacted researchers in the field. All randomized, controlled trials that aimed to alter BP in acute ischemic stroke or acute primary intracerebral hemorrhage were included; treatment had to be initiated within 1 week of stroke onset. Uncontrolled studies, controlled studies involving only active comparators, and studies of patients with subarachnoid hemorrhage were excluded.

Data on early and late case fatality, early neurological deterioration, late disability/dependency, stroke recurrence, quality of life, discharge site, hospital costs, baseline and on-treatment BP, and heart rate were sought, ideally by intention to treat. Methodological quality of the trials, especially relating to concealment of allocation, was also assessed. Data were analyzed using RevMan 5; OR with random-effects model for binary data and weighted mean difference for continuous data each with 95% CIs, were calculated.

### Main Results

Twelve trials involving 1153 participants (range, 15 to 404) were included (603 active, 550 placebo/control). The trials mostly tested drugs that lower BP: angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists (ARA), calcium channel blockers, clonidine, glyceryl trinitrate/nitroglycerine, thiazide diuretics, and mixed antihypertensive therapy. One trial tested phenylephrine (sympathomimetic).<sup>2</sup> At 24 hours after

randomization (Figure), the antihypertensive agents lowered BP: angiotensin-converting enzyme inhibitors weighted mean difference  $-6/-5$  mm Hg (95% CI,  $-22$  to  $10/-18$  to  $7$ ), ARA  $-3/-3$  mm Hg (95% CI,  $-7$  to  $2/-6$  to  $0.4$ ), intravenous calcium channel blockers  $-32/-13$  mm Hg (95% CI,  $-65$  to  $1/-31$  to  $6$ ), oral calcium channel blockers  $-13/-6$  mm Hg (95% CI,  $-43$  to  $17/-14$  to  $2$ ), glyceryl trinitrate/nitroglycerine  $-10/-1$  mm Hg (95% CI,  $-18$  to  $-3/-5$  to  $3$ ), and mixed antihypertensives  $-11$  mm Hg (95% CI,  $-14$  to  $-8$ ). Phenylephrine nonsignificantly increased BP by  $21/1$  mm Hg (95% CI,  $-13$  to  $55/-15$  to  $16$ ). Functional outcome (OR, 1; 95% CI, 0.8 to 1.5) and death (OR, 0.7; 95% CI, 0.4 to 1) were not altered by any of the drugs; data on the other outcomes were not available.

### Discussion

Twelve small trials, involving 1153 participants with either ischemic stroke or primary intracerebral hemorrhage, of deliberate BP alteration in acute stroke have been reported to date. Of the vasoactive drugs studied, angiotensin-converting enzyme inhibitors, ARA, calcium channel blockers, glyceryl trinitrate/nitroglycerine, and combined antihypertensive therapy lowered BP over the first 24 to 48 hours of treatment. Phenylephrine tended to increase BP at 24 hours. Insufficient data were present to assess the effect of changing BP on functional outcome. However, several large trials are assessing whether blood pressure should be lowered or not, including with an ARA (Scandinavian Candesartan Acute Stroke Trial), glyceryl trinitrate/nitroglycerine (Efficacy of Nitric Oxide in Stroke) or "usual therapy" (Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial 2).<sup>3-5</sup>

### Conclusion

There is insufficient evidence to evaluate the effect of altering BP on outcome during the acute phase of stroke. In patients with acute stroke, calcium channel blockers, angiotensin-converting enzyme inhibitors, ARA, and glyceryl trinitrate/nitroglycerine each lower BP, whereas phenylephrine has vasopressor properties.

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From the Stroke Trials Unit, University of Nottingham, Nottingham, UK.

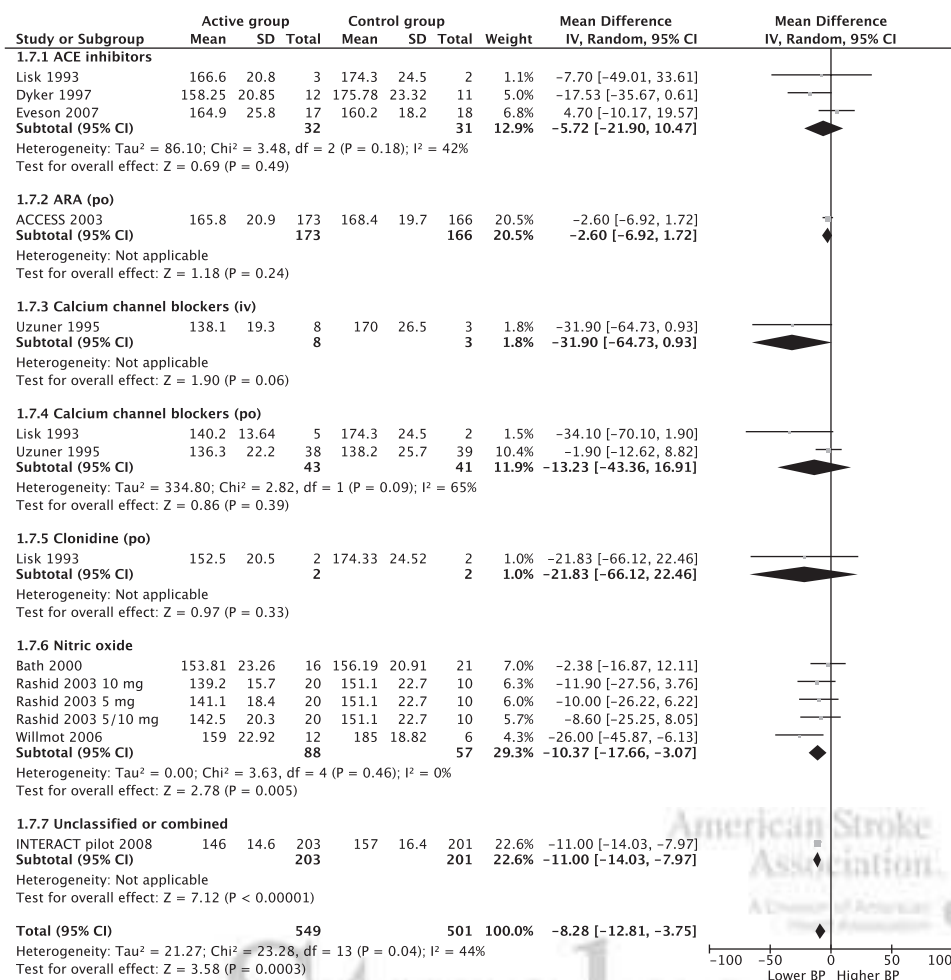
Correspondence to Philip M.W. Bath, MD, FRCP, Division of Stroke Medicine, University of Nottingham, Nottingham City Campus, Nottingham, NG5 1PB, UK. E-mail philip.bath@nottingham.ac.uk

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**Figure.** Forest plot showing the effect of different BP-lowering drugs on systolic BP at 24 hours.

## Implications for Practice and Future Research

The data from the trials included in this review are too limited to provide reliable guidance on whether it is safe and effective to actively lower or raise BP in patients with acute stroke or, indeed, the precise effects this will have on BP. Large randomized, controlled trials of BP management addressing issues such as whether BP be elevated or lowered, the type of treatment, time of treatment initiation, treatment duration, and whether prestroke antihypertensive therapy be continued or stopped during the acute phase of stroke, are required. Several large trials addressing these issues are currently ongoing.

## Disclosures

The authors were involved with 3 completed trials that are included in this systematic review. They are coordinating an ongoing Phase III trial (Efficacy of Nitric Oxide in Stroke) and a Phase II trial of an ARA (telmisartan). P.B. is Stroke Association Professor of Stroke Medicine.

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**KEY WORDS:** acute stroke ■ blood pressure ■ randomized controlled trial